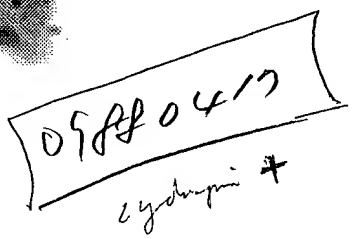


TSG-p53® Knockout Mice (Tumor Suppressor Gene Deficient)

B6.129-*Trp53*^{tm1} N4 and B6.129-*Trp53*^{tm1} N5

Formerly C57BL/6Tac-*Trp53*^{tm1} N4 and C57BL/6Tac-*Trp53*^{tm1} N5

Order Model #'s:

P53N4-M (homozygotes)
P53N5-T (heterozygotes)
P53N5-W (wild type)

Coat Color: Black

Features: The TSG-**p53 mice** are deficient in the *Trp53* tumor suppressor gene. Recent studies indicate that the *Trp53* gene is the most commonly mutated gene in human cancers. This mouse can be used to study *Trp53* gene function, tumor biology or screen potential carcinogens.

Origin: Developed by Donehower and Bradley at the Baylor College of Medicine. Received at Taconic from the Bradley Lab in November 1991 at two backcrosses (N2) onto C57BL/6J from the (129/Sv x C57BL/6) chimera. Bred to N3 prior to cesarean derivation in December 1991 and to N4 immediately after derivation. Homozygote colony maintained at N4 through intercrossing of homozygous males and heterozgyous females.

Heterozygote colony maintained at N5 through mating of N4 Homozygotes with C57BL/6NTac **mice**. Wild type control colony maintained at N5 through mating of N4 Wild Types with C57BL/6NTac **mice**.

Initial Publication: Donehower, L.A., Harvey, M., Slagle, B.L., McArthur, M.J., Montgomery, C.A. Jr., Butel, J.S., Bradley, A. (1992) *Mice deficient for p53 are developmentally normal but susceptible to spontaneous tumors,* Nature, Vol. 356, pp. 215-221.

Updates:
New Applications:
Chromosomal Recombination in Tumor Development
Transgenic Animals for Carcinogenicity Testing
New Results:
Short-term Carcinogenicity Test
Redfield Laboratories Performing Carcinogenicity Studies
New Data: P-cresidine Positive Control

Links to Related Sites:
NIEHS Use of **p53 Mice** for Rapid Identification of Potential Carcinogens
Alternatives to Carcinogenicity Testing - ILSI/HESI Committee

Reference Library:
Use of Transgenic Models in Proposed Carcinogenicity Bioassay
Spontaneous Proliferative Lesions, Organ Weights, Body Weights

Health Reports by Health Report Group:
MBU 3A

Related Animal Models:
C57BL/6 TSG-**p53** N12 Knockout **Mice**
TSG-**p53**®/Big Blue®Knockout/Transgenic **Mice**
TG.AC Transgenic **Mice**
XPC Knockout **Mice**
pim-1 Microinjected **Mice**

Taconic Transgenic Models are produced in Isolated Barrier Unit (IBU™) facilities under MPF™ conditions, and shipped in Taconic Transit Cages (TTC™).

Home / Health Reports / Technical Library / Search / Contact Taconic

NCBI Genes and disease Map

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y

NEW **Genome View**

p53 gene
on chromosome 17

Databases

PubMed
the literature

LocusLink
collection of gene-related information

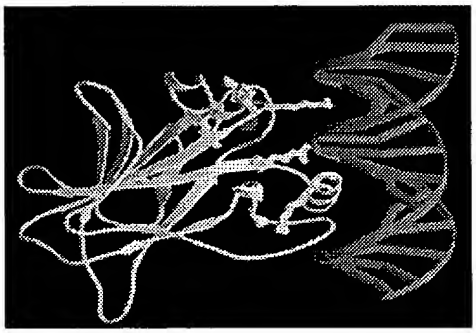
Protein structure
molecule in 3D

OMIM
catalog of human genes and disorders

Information

CancerNet
from the National Cancer Institute, NIH

THE p53 GENE like the Rb **gene**, is a tumor suppressor **gene**, i.e., its activity stops the formation of tumors. If a person inherits only one functional copy of the **p53 gene** from their parents, they are predisposed to **cancer** and usually develop several independent tumors in a variety of tissues in early adulthood. This condition is rare, and is known as Li-Fraumeni syndrome. However, mutations in **p53** are found in most tumor types, and so contribute to the complex network of molecular events leading to tumor formation.



The structure of the core domain of the p53 protein (light blue) bound to DNA (dark blue) The six most frequently mutated amino acids in human cancers are shown in yellow - all are residues important for p53 binding to DNA. Red ball: zinc atom. [Reproduced from Cho, Y., et al. (1994) Science, 265, 346-355, with kind permission.]

The **p53 gene** has been mapped to chromosome 17. In the cell, **p53** protein binds DNA, which in turn stimulates another **gene** to produce a protein called p21 that interacts with a cell division-stimulating protein (cdk2). When p21 is complexed with cdk2 the cell cannot pass through to the next stage of cell division. Mutant **p53** can no longer bind DNA in an effective way, and as a consequence the p21 protein is not made available to act as the 'stop signal' for cell division. Thus cells divide uncontrollably, and form tumors.

Help with unraveling the molecular mechanisms of cancerous growth has come from the use of mice as models

cancerous growth has come from the use of mice as models for human **cancer**, in which powerful '**gene** knockout' techniques can be used. The amount of information that exists on all aspects of **p53** normal function and mutant expression in human cancers is now vast, reflecting its key role in the pathogenesis of human cancers. It is clear that **p53** is just one component of a network of events that culminate in tumor formation.

Federal Register Announcement, NIH, Late November 1995

Text of a *Federal Register* notice released by the Office of Technology Transfer, NIH, on November 24, 1995.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health

ACTION: Notice

The inventions listed below are owned by agencies of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for U.S. companies and may also be available for licensing.

ADDRESS: Licensing information and copies of the U.S. patent applications and issued patents listed below may be obtained by writing to John Fahner-Vihtelic, Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Box 13, Rockville, Maryland 20852-3804 (telephone 301/496-7735 ext 285; fax 301/402-0220). A signed Confidential Disclosure Agreement (CDA) will be required to receive copies of the patent applications. Requests for copies of issued patents do not require the execution of a CDA.

Methods For Determining The Presence Of Functional p53 In Mammalian Cells
Fornace, A.J., Kastan, M.B. (NCI)

Filed 10 Aug 94
Serial No. 08/288,872 (CON of 07/974,960)
The protein p53 is involved in tumorigenesis. Recent observations have indicated that the gene encoding p53 is a tumor suppressor gene; however, mutation or deletion of this gene results in loss of this suppressor function. Mutations of the p53 gene have been demonstrated in tumors of the colon, breast, lung, ovary, bladder, and other organs, making the p53 gene the most commonly mutated gene yet identified in human cancers. While currently used assays can detect the presence of wild-type or mutant p53 protein in mammalian cells, they cannot accurately determine the presence of functional p53 protein in these cells, which is necessary to determine the biological function of functional p53 and to develop subsequent diagnostic modalities using functional p53. This invention describes a specific gene whose expression is dependent on the presence of functional p53 in cells and tumors, as well as methods by which the presence of this gene may be detected. It also describes a diagnostic kit utilizing a nucleic acid sequence capable of binding functional p53, which is then measured to detect p53 presence. Issuance of a patent on this invention is currently pending. [portfolio: Cancer - Diagnostics]

Novel B-Lymphoma Cell Line And Antigen
Bock, G.H., Nelson, D.L., Kurman, C.C., Fleisher, T.A. (NCI)
Filed 9 Aug 94
Serial No. 08/287,718 (FWC of 07/934,106)
Various cell lines of B-cell lineage have been produced, but none have been of tumor cell origin. This case provides an IL-6 dependent B-cell lymphoma cell line, designated DS-1. The invention further provides a monoclonal antibody which reacts with the cell line and a method for detecting the presence of neoplastic cells by detecting the presence of an antigen on a cell which is not normal for that cell type. [portfolio: Cancer - Diagnostics; Cancer - Research Reagents]

Novel Human ras-Related Oncogenes Unmasked By Expression cDNA Cloning
Aaronson, S., Chan, A., Miki, T. (NCI)
Filed 24 May 94
Serial No. 08/247,946
A family of small G-proteins encoded by H-, K-, and N-ras is frequently activated as oncogenes in a wide variety of human tumors. Activation is usually due to a point mutation within the coding sequence which results in the molecule to be constitutively in the GTP bound (active) state. In normal cells, these proteins are coupled to growth factor signaling pathways and appear to cause proliferation or differentiation. Over the past several years, cloning efforts by many laboratories have

greatly expanded the number of ras-related proteins, to include R-ras, K-rev-l/rap and TC21. The present invention relates to a mutant TC21 protein that was cloned from an expression cDNA from a ovarian carcinoma cell line. Based upon the finding that an oncogenic form of TC21 exists, the present invention also relates to the generation of point mutations in R-ras for expression study. The present invention also relates to methods of diagnosing cancers or monitoring disease progression by detecting mutant forms of R-ras or TC21 at the protein or gene level. [portfolio: Cancer - Diagnostics; Cancer - Research Reagents]

Immortalized Adult Human Prostate Epithelial Cell Lines
Rhim, J.S., Webber, M.M. (NCI)
Filed 28 Apr 94
Serial No. 08/234,843
This invention relates to cell lines which are useful in testing compounds for anti-carcinogenic, anti-neoplastic, anti-invasive, or anti-metastatic activity by growing the cell line in the presence of the subject compounds. The cell lines contain DNA of a human Papilloma virus (HPV), either alone or with an activated viral ras oncogene, e.g., v-Ki-ras. The HPV immortalized line is not tumorigenic; however, the V-Ki-ras transformed HPV cell line is tumorigenic. They are useful for determining causes, treatment, and prevention of prostate cancer, benign prostate hyperplasic, male infertility, birth defects, aging, and assessment of environmental toxic agents. [portfolio: Cancer - Research Reagents]

Phosphonoalkyl Phenylalanine Compounds Suitably Protected For Use In Peptide Synthesis
Burke, T.R, Smyth, M.S., Lim, B.B. (NCI)
Filed 8 Jun 93
Serial No. 08/073,088
A novel class of phosphononodifluoromethyl phenylalanine ("F2Pmp") derivatives have been developed which are suitable for the synthesis of peptides containing the phosphotyrosyl (pTyr) mimetic, F2Pmp. These analogues bear Boc or Fmoc protection at the Nγ-position for either solution or solid-phase peptide synthesis using standard techniques. A number of studies have shown that peptides containing the F2Pmp residue show utility as inhibitors of src homology 2 (SH2) domain binding interactions and of phosphotyrosyl phosphatases. Unlike pTyr residues, the F2Pmp moiety is stable to both chemical and phosphatase-mediated hydrolysis, making it an attractive replacement for pTyr in signal transduction peptides. [portfolio: Cancer - Research Reagents]

Monoclonal Antibodies To Prostate Cells
Pastan, I. (NCI)
Filed 8 Oct 92

Serial No. 07/958,140
Monoclonal antibodies which bind to an antigen associated with prostate cells, including prostate cancer, can be used either individually or conjugated to drugs, labels, radioisotopes, or cytotoxins to target delivery of the conjugated to prostate cells. The antibodies are thus useful in a variety of diagnostic and therapeutic applications involving prostate cancer. A hybridoma cell line secreting monoclonal antibody PR1 is also provided, as well as methods for screening for the presence of metastatic prostate cancer. [portfolio: Cancer - Therapeutics]

Antibodies To Human LINE-1 p40 Protein
Fanning, T.G. (NCI)
Serial No. 07/750,044
Patent Issued 18 Jan 94
U.S. Patent No. 5,280,108
Antibodies to the human LINE-1 retrotransposon offer a powerful new tool for studying tumors. In most cell lines and tissues, human LINE-1 sequences (LIHs) are not expressed; however, LIH-specific RNA and proteins have been detected in cell lines and tissues derived from human germ cell tumors (teratocarcinomas) and breast tumors. These LIH antibodies, which are specific for the p40 protein portion of the retrotransposon, can be used for determining LIH expression in tumor cells and determining the role this retrotransposon plays in these cells. [portfolio: Cancer - Research Reagents]

Cartilage-Derived Morphogenetic Proteins
Luyten, F.P., Moos, M. Chang, S. (NIDR)
PCT Application PCT/US94/12814 filed 7 Nov 94
DHHS Reference No.: E-138-94/0
The present invention provides a cartilage-derived extract which initiates and promotes ectopic cartilage and bone development in vivo and recombinant cartilage-derived morphogenetic proteins which promote development of musculoskeletal tissues in vivo. These products will be useful in the therapeutic induction, repair, and maintenance of skeletal tissues. These compounds show promise for the healing of joint surface lesions and repair or reconstruction of cartilaginous tissues. They are also useful as growth factors for cells of the chondrocyte lineage which, expanded ex vivo, can be implanted into an individual where cartilage growth is desired. In addition, cloned polynucleotides encoding these proteins will be effective diagnostic reagents for detecting genetic abnormalities associated with poor skeletal development. [portfolio: Cancer - Therapeutics, biological response modifiers, growth factors]

Pulsed Low Frequency EPR Spectrometer And Imager
Bourg, J., Cherukuri, M., Mitchell, J., Mirotznik, M., Roth, B.,

Subramanian, S. (NCI)
Serial No. 08/097,811
Patent Issued 7 Feb 95
U.S. Patent No. 5,387,867
This application describes an Electron Paramagnetic Resonance (EPR) spectroscopy imaging system. This system generates broadband pulses having a RF carrier frequency that is not highly absorbed by biological materials. The pulse generating system includes up and down chirp converters for frequency modulating of a carrier frequency and compression of the frequency modulated pulse to form a broadband excitation pulse of high energy. This technology's function has been proven and could form the basis of a clinical imaging device capable of high sensitivity to free radical species in human patients.
[portfolio: Devices/Instrumentation - Diagnostics, electron paramagnetic resonance]

Federal Register Announcement, NIH, Late November 1995

Text of a *Federal Register* notice released by the Office of Technology Transfer, NIH, on November 24, 1995.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
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ADDRESS: Licensing information for the technologies referenced below may be obtained by contacting Stephen Finley, Ph.D., at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804 (telephone 301/496-7056 ext 215; fax 301/402-0220).

cDNA Sequence of a Clone Encoding Arylalkylamine N-acetyltransferase

Klein et al. (NICHD)
DHHS Reference No. E-161-95/0 and
Human Gene Encoding Serotonin N-acetyltransferase
Klein et al. (NICHD)
DHHS Reference No. E-222-95/0
The identification of an arylalkylamine N-acetyltransferase (AA-NAT) mRNA in the brain and the cloning of ovine and human cDNAs encoding for the pineal enzyme serotonin N-acetyltransferase. These findings open a new area of researchœthe importance of AA-NAT in the regulation of brain serotonin and the development of drugs which raise serotonin levels by inhibiting this enzyme. This enzyme is the rate-controlling step in the conversion of serotonin to melatonin. The hormone melatonin has been linked to controlling circadian rhythms. Development of regulators of the synthesis of the hormone melatonin may be the preferred route to controlling seasonal reproduction cycles or sleep cycles of vertebrates. Activators of the serotonin N-acetyltransferase may be beneficial to induce or enhance the quality of sleep at night. Inhibitors of serotonin N-acetyltransferase may lead to drugs that stimulate the levels of alertness and physical activity or delay the onset of fatigue. Licenses for the cDNAs encoding for this enzyme or the production of the enzyme are available.